

The effect of pediatric traumatic brain injury on simulated transcranial direct current stimulation electric field

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Synopsis:

By the age of 10, 16% of children sustain at least one brain injury requiring medical attention, where approximately 25-30% have long-term cognitive problems. Transcranial direct current stimulation (tDCS) can improve cognitive function after traumatic brain injury, but its effectiveness may be limited by structural brain damage. Using simNIBS, we simulated group differences in tDCS electric field in children with mild, moderate-severe TBI and healthy controls (T1 scans). Electric field strength did not significantly differ between groups. Thus, structural damage after pediatric TBI does not affect tDCS efield, providing confidence in using consistent tDCS intensity across TBI severities. Future work should use diffusion tensor data to explore effects of microstructural damage on electric field.

Background:

By the age of 10, 16% of children will sustain at least one traumatic brain injury (TBI) requiring medical attention (Langlois et al., 2006). Even following the mildest injury (mild TBI/concussion), 25-30% of these children experience chronic problems (Ewing-Cobbs et al., 2018). Attention and concentration problems are among the most common cognitive symptoms following TBI (Ahmed et al., 2017). Although medications are often prescribed to improve symptoms, these are associated with potential side-effects and stigma in childhood which limit compliance (Charach et al., 2006). Transcranial direct current stimulation (tDCS) is a type of non-invasive brain stimulation technique which may improve attention following TBI (Li et al., 2019; Eilam-Stock et al., 2020). It is important, however, to understand the effect of tDCS on a child with brain injury, given the injury-induced changes in brain structure and function (Li et al., 2019), especially during this time of rapid neurological development (Iyer et al., 2019). Brain modelling software such as simNIBS (Saturnino et al., 2019) allows simulation of tDCS experiments using unique MRI-based head models to assess how damage sustained during pediatric TBI may affect tDCS current flow (Thielscher et al., 2015). Diffuse axonal injury in TBI causes scarring and gliosis, which increases tissue resistivity, therefore increasing tDCS electric field strength and potentially shunting the movement of tDCS current (Datta et al., 2010). simNIBS can provide insight into whether the degree of anatomical structural damage to brain networks affects tDCS electric field in children with TBI.

Methods

This study evaluated the simulated tDCS electric field in children with mild (mTBI), moderate-severe (mod-sev) TBI and healthy controls (HC). We hypothesised that mod-sev TBI patients would display the highest electric field due to decreases in tissue conductivity after damage. Two convenience samples with T1 MRI scans were used: mTBI and HC participants were

sourced from the PLAYGAME trial (Barlow et al., 2014) (3 T GE Healthcare Discovery scanner), and mod-sev TBI participants from the Acquired Brain Injury in Children Research Program (Brisbane, Australia; 3 T Siemens Prisma scanner). Individual head models were created using the headreco pipeline (Nielsen et al., 2018) (simNIBS version 3.2, Copenhagen) (Thielscher et al., 2015) in MATLAB (R2020b, Massachusetts: The MathWorks, Inc) from T1 scans of 17 children with mTBI (mean age 13.6 ± 3.0 years; one-month post-injury), 9 mod-sev TBI (13.1 ± 3.1 years, 6 ± 4.1 years post-injury) and 17 HCs (14.3 ± 3.3 years). tDCS was modelled using the F3-anode/F4-cathode (10-20 EEG) montage. Electrode size was set to 5x5 cm, 4 mm thickness. Electrode y-axis pointed towards FC3 and FC4 for F3 and F4 electrodes, respectively (dorsolateral prefrontal cortex, dlPFC). Current intensity was 1 mA (anode) and -1 mA (cathode), and conductivity was as per default simNIBS settings. Average electric field (E_{norm}) was calculated using the standard simNIBS pipeline (Saturnino et al., 2019). The e-field distribution map was visualised using gmsh (Geuzaine and Remacle, 2009). Demographics and group level differences in whole brain E_{norm} and left dlPFC region of interest (ROI) were analysed using regression in SPSS Statistics software (IBM Corporation Version 28, Armonk, NY).

Results

There were no significant differences in age or pre-injury symptom scores between groups (age: one-way ANOVA, $F(2,40) = 1.38$, $p = 0.265$; pre-injury symptom scores (PCSI): one-way ANOVA, $F(2,40) = 2.19$, $p = 0.150$). Males were over-represented in the mod-sev TBI group ($\chi^2 = 7.17$, $p = 0.028$). Visual inspection of electric field models indicated a higher and broader electric field across the prefrontal cortex in mod-sev TBI, compared to mTBI and HCs (see Figure). The overall maximum value of mean electric field was highest in the mod-sev TBI group (0.83 v/m) compared to maximums of 0.71 v/m in the mTBI and 0.41 v/m in the HC groups. This supported our hypothesis that decreases in tissue conductivity in mod-severe TBI would increase electric field. After controlling for age, sex, and scanner, however, linear regression found no effect of group on whole-brain mean electric field (E_{norm}): mod-sev = 0.07 (SD 0.013) v/m, mTBI = 0.06 (SD 0.012) v/m, HC = 0.06 (SD 0.013) v/m; [$R^2 = 0.152$, $p = 0.169$]. Given the role of the left dlPFC as the hub for the executive network, and because our stimulations were conducted over the left and right dlPFC (anode and cathode, respectively), we conducted a region of interest analysis in the left dlPFC. Similarly, we found no effect of TBI group on the mean electric field strength in the left dlPFC: mod-sev TBI = 0.17 (SD 0.076) v/m, mTBI = 0.13 (SD 0.026) v/m, HC 0.14 (SD = 0.030) v/m; [$R^2 = 0.154$, $p = 0.164$].

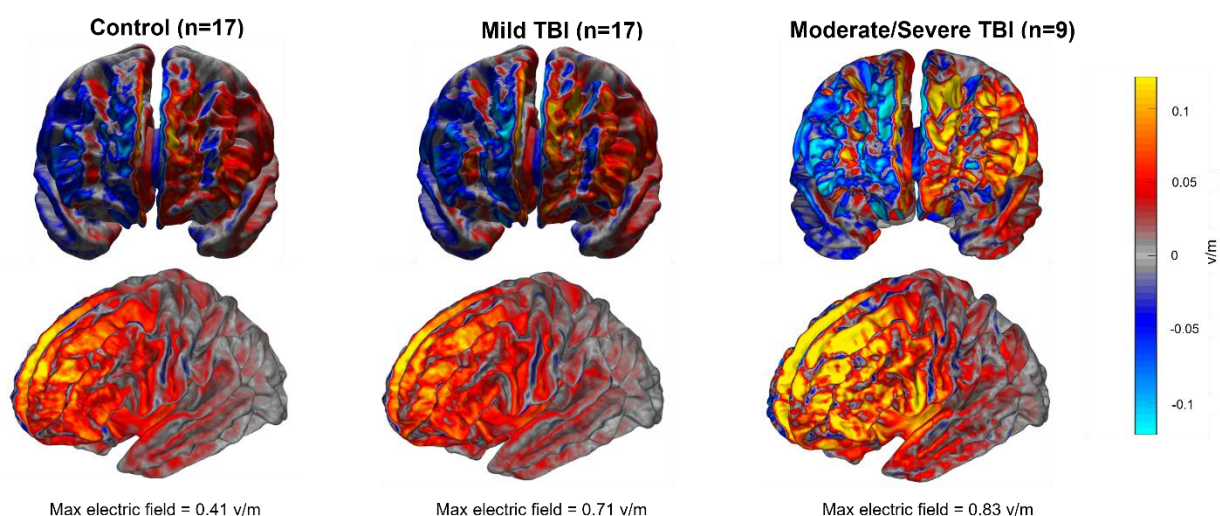


Figure 1. Simulated tDCS electric field in healthy controls (HCs), mild TBI (mTBI) and moderate-severe (mod-sev) TBI using simNIBS. Electrodes modelled as 5x5 cm squares (saline and sponge, 4 mm thickness), placed on F3/F4 (anode/cathode), with FC3/FC4 orientation, respectively, according to 10/20 EEG system. tDCS intensity set to 1 mA. Colour bar indicates electric field (v/m), ranging from -0.1 to 0.1.

Discussion

Our modelling indicates that the degree of anatomical structural damage following pediatric TBI is unlikely to significantly alter electric field during tDCS. This may be due to the relative insensitivity of T1 anatomical scans to white matter injury and microstructural damage. The increased electric field strength and broader distribution of electric field in the mod-sev TBI group (Fig. 1) may reflect scarring and gliosis, which causes increased tissue resistance and thus electric field strength (Datta et al., 2010). Notably, measured electric fields were well within recommended safety levels across all groups (maximum 80-120 v/m) (Bikson et al., 2016), with a maximum electric field of 0.83 v/m in the mod-sev TBI group. Further, the electric fields reported in this study were consistent with previous tDCS modelling studies (Caulfield et al., 2022; Mizutani-Tiebel et al., 2022). Our study was limited by the use of T1, rather than diffusion data, which is more sensitive to white matter injury and microstructural damage. Although MRI scans were acquired using two different scanners, which could have affected comparison, the lack of effect of scanner in regression analyses suggests that this was unlikely. Overall, our simulations provide greater confidence in the application of existing tDCS paradigms (created in healthy populations) to children with TBI. Future research should use diffusion tensor imaging to model the effect of microstructural damage following pediatric TBI on tDCS electric field.

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Disclosures

Nothing to disclose by any authors.